Stress Induced Gastric Ulcers: Presenting as Massive Rectal Bleeding in a Newborn

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ABSTRACT

Severe gastrointestinal bleeding in newborn period is a serious but uncommon phenomenon that has a broad differential diagnosis. Primary duodenal ulcers are rare in children but stress induced ulceration in stomach occurs more often in neonatal period due to birth asphyxia, prolonged labour, cesarean deliveries, instrumentations, respiratory distress syndrome and sepsis. These present as acute onset of gastrointestinal bleeding commonly as altered gastric aspirate, hematemesis or malena. We report a case of a neonate with stress induced gastric bleeding following birth asphyxia who presented with massive gastrointestinal bleed manifesting as hematemesis and massive rectal bleeding. Resuscitation with multiple blood transfusion and parenteral use of ranitidine controlled the bleeding. Stress induced gastric ulcers should be suspected in a neonate presenting with massive gastrointestinal bleeding after difficult delivery and birth asphyxia.

KEY WORDS

Birth asphyxia, massive rectal bleeding, newborns, stress ulcers

INTRODUCTION

Stress induced ulceration in the stomach occurs more often in the neonatal period.[1] Gastric bleeding from stress ulcers is a known entity in neonates.[2] These occur in the newborns but arise secondary to serious underlying illness.[1] Such peptic ulcers are also reported with birth asphyxia, prolonged labour, cesarean deliveries, respiratory distress syndrome, instrumentations, and sepsis.[3] The differential diagnosis includes coagulopathies such as hemorrhagic disease of the newborn, milk protein allergy, sepsis, inherited bleeding disorders, necrotizing enterocolitis (NEC), intussusception, and vascular anomalies. We report a case of a newborn with stress induced gastric bleeding following birth asphyxia who presented with massive gastrointestinal (GI) bleed manifesting as hematemesis and massive rectal bleeding.

CASE REPORTS

A 2.09 kg baby boy born to a 23 years old primi gravida lady at term (Ballard score 38 weeks) after a non-consanguineous marriage delivered by emergency cesarean section in a nearby hospital for perinatal asphyxia was referred to our center at six hours of life for neonatal intensive care (NICU) and further management as meconium aspiration syndrome. Baby had received prophylaxis Inj. Vitamin K 1 mg intramuscularly at birth. On arrival baby was found to be lethargic with heart rate of 120 beats/min, respiratory rate of 58 breaths/min, Blood pressure of 60/36 mmHg (mean 48 mmHg), and oxygen saturation of 95% on head box oxygen 6 L/min. Systemic evaluation was normal except for a patent ductus arteriosus (~1.5 mm) with left to right shunt which was confirmed by echocardiography. Baby was managed conservatively with IV fluids and antibiotics. Chest x-ray showed B/L hyperinflated lungs with diffuse infiltrations, suggestive of meconium aspiration, however hematological investigations sent was within normal range. Oxygen was gradually tapered and weaned off within 72 hours. Trophic feeding with expressed breast milk was introduced via nasogastric (NG) tube, and in view of isolated patent ductus arteriosus loading dose of oral Ibuprofen (10 mg/kg) was given via NG tube on the 3rd day of life prophylactically. On the 4th day of life baby showed deterioration with subtle siezures, hypoglycemia and hyponatremia, baby became

pale and desaturated requiring mechanical ventilation and ionotropic supports. One episode of fresh blood vomitus (~10 ml) was observed and blood mixed gastric fluid aspirated from NG tube (~5 ml). Baby was kept nil per oral. Ibuprofen was discontinued. One dose of Inj. Vitamin K was repeated and fresh blood transfused. Hematological investigation showed drop in hemoglobin level to 8.40 gm/dl (Initial 12.10 gm/dl), prothrombin time 18 seconds (INR: 1.34), Activated partial thromboplastin time 46 seconds (reference range 24-32 seconds), platelets $136X10^3$ /cumm, CRP <5 mg/L, liver function test was normal and blood culture was negative. Abdominal x-ray and ultrasonography was normal. In view of sudden deterioration transcranial ultrasonography was also done which showed no signs of intracranial hemorrhage. Inj. Ranitidine was added with the suspicion of stress induced gastric ulcer bleeding. Upper GI endoscopy was not done due to the inavailability of neonatal endoscopy in our center. Upper GI bleeding gradually decreased after starting of ranitidine, two times of fresh blood and three times of fresh frozen plasma transfusion, NG aspirate gradually became clear with no blood seen in gastric aspirate after 5 days of treatment, hemoglobin level improve to 13.10 gm/dl and hence ranitidine was discontinued gradually after seven days of treatment. After two days of stopping ranitidine, bloody NG aspirate and two episodes of passage of massive fresh blood (15-20 ml/episode) was noticed per rectum. No anal fissures were seen, abdomen was soft and not distended, there were no features suggestive of NEC or sepsis. Stool culture was re sent which also did not show growth of any organism. Hemoglobin dropped to 8.70 gm/dl. One dose of Inj. Vitamin K was repeated, fresh frozen plasma and fresh blood was again transfused. Ranitidine was restarted. After multiple episodes of fresh blood and fresh frozen plasma transfusion, rectal bleeding gradually decreased. After ten days of restarting ranitidine, repeated stool examination showed negative for occult blood. Hemoglobin improved to 15.10 gm/dl. NG feeding was restarted. No further bleeding was noticed. The baby was ventilated for 32 days. During the NICU stay extubation was attempted four times which was unsuccessful and needed re-intubation. Repeated transcranial ultrasonography showed features of severe brain atrophy suspected to be due to perinatal asphyxia, however there was no evidence of intracranial hemorrhage. In view of unsatisfactory improvement and poor prognosis of the baby, parents refused for further treatment and withdraw all the life supports on the 35th day of NICU stay.

DISCUSSION

Peptic ulcers are rare during neonatal period and infancy. These occur in the newborns but arise secondary to serious underlying illness.[1] Such peptic ulcers are reported with birth asphyxia, prolonged labour, cesarean deliveries, respiratory distress syndrome, instrumentations and sepsis.[3] All risk factors increase the severity of the illness also in the neonatal context and there by aggravate the stress itself. In few studies of children treated in intensive care the frequency has been defined without endoscopy and has varied from 5% to 25%.[4] The lesions are likely to bleed if blood coagulation is somehow disturbed, for that reason the newborn are especially prone to bleed.[5] During continuous exposure to a risk factor such as mechanical ventilation for several weeks the lesions spread and become deeper, forming ulcers and erosions which eventually lead to perforations. In infants the first description of this kind of gastric lesions was published by Liebman et al.,[6] since then there have been several case reports on ulcers and erosions in infants treated in NICU. Our patient had a cesarean delivery, birth asphyxia, mechanical ventilation, electrolyte imbalance and neonatal seizures as stressful factors possibly which was precipitated by the use of Ibuprofen which we believe may have lead to the massive upper GI bleeding.

These ulcerations have been shown to have acute onset of GI bleed presenting most commonly as altered gastric aspirate, hematemesis or melena. Our patient presented with massive upper GI bleed as hematemesis and hematochezia. In a varying percentage of patients stress ulceration leads to clinically significant GI haemorrhage. Hence, especially in infants, once stress ulcers do cause significant haemorrhage, the likelihood of mortality approaches 40%.[7] Massive upper GI bleeding is associated with increased mortality. Judging from the findings in adults, it takes considerable time for the lesions to progress to perforation, while reports on newborns mostly merely describe gastric perforations in severely ill newborns.[8]

These ulcers have been widely attributed to the circulatory disturbances of the GI tract at the time of prolonged or difficult labour. The asphyxia results in reflex vasospasm leading to duodenal congestion and possibly mucosal ischemia causing devitalisation of the mucus membrane with subsequent peptic digestion of the damaged area. It has also been described that the compression of duodenum between the liver and the head of the pancreas during birth may result in ischemia of duodenum and mucosal hemorrhage.[9] Any physiological stress impairs the ability of the intact gastric mucosa to maintain homeostasis and results in the formation of multiple superficial gastric erosions. Mucosal injury is present within hours of stressful events. On endoscopic examination performed in adult patients treated in intensive care, multiple gastric erosions have been observed in all patients within 72 hours of admission to intensive care.[10] Gastric acid production starts in term and preterm babies soon after birth and probably contributes to the pathophysiology of stress ulcers.[11]

Several etiologies have been suggested for rectal bleeding in newborns. Swallowed maternal blood at the time of delivery or from cracked nipples during breast feeding is the most common cause of suspected GI bleeding in the

neonate.[12] Anal fissures and maternal blood digestion remain a differential diagnosis for an isolated rectal bleeding event, but can be excluded with a simple physical examination of either the infant or the mother. In our patient there were no anal fissures and mother did not have a cracked nipple, however the baby was not under breast feeding. In the past, the most common etiology was believed to be a hypersensitivity reaction of the bowel mucosa to digested antigens, primarily to the protein in cow's milk.[13] Sepsis and NEC is commonly suspected in a newborn presenting with bloody stool. NEC is present in 1–7% of NICU admissions with a frequency of 16.9 per 1000 premature neonates. In term neonates NEC is relatively uncommon, accounting for less than 10% of NEC cases.[14] Our patient received routine prophylactic antibiotics, an intervention that could have reduced the prevalence of septicemia and thrombocytopenia, however the septic screening sent were normal and there were no clinical and radiological features suggestive of NEC. Our patient had received routine vitamin K injection on delivery and was repeated following GI bleeding, a factor that could have reduced the risk of bleeding due to deficiency of vitamin K dependent clotting factors. In addition, the family history was unremarkable for bleeding diathesis and any drug intake. Oral Ibuprofen is used in our unit for the closure of patent ductus arteriosus because its efficacy has been shown to be comparable to that of Indomethacin, without reducing mesenteric, renal and cerebral blood flows. Non-steroidal anti-inflammatory drugs are well known to be a predisposing factor for bleeding, but it has not been shown to be a risk factor for rectal bleeding or NEC in preterm infants.[15]

The development of the new fiberoptic technique has made endoscopies possible also in newborns and even in very low birth weight infants.[16] This advance has made it possible to demonstrate that these infants have gastric lesions early during intensive care. Such lesions may have an effect on mortality and morbidity. The technical advancement in upper GI endoscopy with smallest diameter scopes have made it easy to define such lesions in infants as erosions, gastric or duodenal ulcers which was not possible earlier.[16] Unfortunately upper GI endoscopy in infants is still not possible in our center, which may have been a major limitation of our case study. Most cases of upper GI bleeding in neonates are benign and self limiting. They usually do not warrant an endoscopy. It may however be of value in cases of acute severe hemorrhage requiring blood transfusion or in unexplained persistent or recurrent bleeding, as in our case.

Histamine-2 (H2) receptor blockers and proton pump inhibitors (PPI) used in the neonatal period have shown to cause healing earlier as compared to placebo.[17] In our patient parenteral ranitidine was used and was given effectively leading to clinical recovery of GI bleeding. As patients recover from the stressful event the erosions gradually decrease in size and depth and usually disappear within 10 to 14 days without significant episodes of bleeding.[18] There are several studies which show definitively that H2-receptor blocking is effective in reducing intragastric acidity as measured by intraluminal gastric pH also in preterm and term infants.[17] H2 blockers have been shown to be effective in increasing gastric pH. Ranitidine has been found to be relatively safe and can control bleeding earlier with no significant untoward side effects.[17] Stress ulcers and upper GI bleeding are frequent complications of critical illness in children admitted to pediatric intensive care units, of whom up to 25% develop GI bleeding or perforation. A gastric pH below 2.5 is one of the risk factors for development of stress ulcers and GI bleeding. Ranitidine is therefore prescribed routinely in pediatric intensive care units for prevention of stress ulcers.[19]

There is evidence of an increased risk of infections and NEC related to the use of H2 blockers and PPIs in neonates. These medications, like many others administered in neonatology, have not been approved by the US Food and Drug Administration for use in this population and are prescribed in an off-label manner because of the perceived safety and potential benefit demonstrated for older populations. Despite these aspects, the use of these drugs has progressively increased. In the NICU, the most common indications for the administration of inhibitors of gastric acid secretion are prophylaxis or therapy of stress ulcers and gastroesophageal reflux disease, but their efficacy in preterm infants is still debated.[20]

CONCLUSION

Stress gastric ulcers should be suspected in a neonate presenting with massive GI bleeding after difficult delivery and birth asphyxia. Resuscitation with blood transfusion and H2 blockers are quite helpful for rapid healing. Identification and treatment of the underlying cause will assist in preventing morbidity and mortality. A variety of surgical and non-surgical diagnosis, congenital deficiencies of coagulation factors that may present with bleeding should also be considered in the differential diagnosis. Ranitidine seems effective and can be administered with care in term and preterm infants.

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